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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

Date: 7/29/2010

Subject: **Oxamyl**. Response to Deficiency; Cotton Gin-Byproduct: Magnitude of Residue Data and Analytical Method.

PC Code:	103801	**DP Barcodes:**	D372355
Decision Nos:	NA	**Registration Nos:**	352-532 & 352-372
Petition No.:	NA	**Regulatory Action:**	NA
Risk Assessment Type:	NA	**Case No.:**	NA
TXR No.:	NA	**CAS No.:**	23135-22-0
MRID No.:	45803801, 46091101 & 46091102	**40 CFR**	§180.303

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Through: Felecia Fort, Branch Chief
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Insecticide/Rodenticide Branch (IRB)/Registration Division (IRB/RD) (7505P)

Executive Summary

Tolerances are established under 40 CFR §180.303 for residues of the insecticide oxamyl, including its metabolites and degradates, in or on apples, bananas, carrots, celery, citrus, cotton, cucumbers, eggplants, garlic, ginger, muskmelon (including cantaloupe and honeydew melon), onion (dry bulb), peanuts, pears, peppers, peppermint, pineapples, plantains, potatoes, pumpkins, soybeans, spearmint, squash, sweet potatoes, tobacco, tomatoes, watermelons, yams, and non-bearing apple, cherry, citrus, peach, and pear to control insects, mites, and/or nematodes. Compliance with the tolerance levels specified above is to be determined by measuring only the sum of oxamyl (methyl N,N -dimethyl- N -[(methylcarbamoyl)-oxy]-1-thiooxamimidate) and its

oxime metabolite (methyl N,N-dimethyl-N-hydroxy-1-thiooxamimidate), calculated as the stoichiometric equivalent of oxamyl, in or on the commodity.
Oxamyl may be applied preplant, at planting, or postemergence on the above crops by foliar treatment using aerial or ground equipment. Oxamyl is sold in the U.S. as a soluble liquid concentrate (SC/L) under the trade name Vydate® by E.I. du Pont de Nemours and Company (DuPont). The 2.0 and 3.77 lbs/gal SC/L formulations are the oxamyl formulations presently registered for food/feed uses.

In response to deficiencies cited in Reregistration Eligibility Decision (RED) Document HED RED Chapter (J. Punzi, DP Barcode: 263849, 3/7/2000), the registrant submitted magnitude of residue studies for cotton gin by-products along with storage stability and analytical method studies.

Conclusion: The sumbitted field trial data and data-collection method for cotton gin byproducts were reviewed in HED and found to be acceptable. This deficiency is now resolved. **A tolerance of 120 ppm on cotton gin-byproducts is now required**. There is no reasonable expectation of finite oxamyl residues of concern in animal commodities [40 CFR, §180.6(a)(3)]. Should the registrant wish to use this analytical method as data-collection for other commodities in future, an acceptable radiovalidation of this method or a side-by-side comparison of this method with GLC enforcement method should be conducted; it is recommended that the registrant conduct such analyses on a plant matrix identified in the plant metabolism studies as the most challenging for analysis.

Detail Consideration:
45803801.der
46091101.der
46091102.der

As a result of changes in Table 1 of OPPTS 860.1000 (7/13/96), the Agency has considered cotton gin byproducts to be a raw agricultural commodity (RAC). Therefore, magnitude of residue studies depicting oxamyl residues of concern in/on cotton gin byproducts resulting from the maximum registered use of oxamyl on cotton were required ((J. Punzi, DP Barcode: 263849, 3/7/2000). In 2000 RED, at least 3 field trials for each type of harvesting (stripper and picker) were required, for a total of 6 field trials. However, Table 1 of OPPTS 860.1000 has been revised in June 30, 2008 and there are only 2 field trials for harvesting of stripper cotton are needed. In the current submission, higher total residues are observed on picker cotton and therefore all field trial data are considered for establishment of tolerance level.

E. I. du Pont de Nemours and Company has submitted field trial data for oxamyl in cotton gin by-products. A total of six field trials were conducted in the United States during the 2001 growing season. The trials took place in Region 2 (1 trial in SC), Region 4 (1 trial in AR), Region 6 (1 trial in OK), Region 8 (2 trials in TX), and Region 10 (1 trial in CA). At each trial, three broadcast applications of Vydate® C-LV Insecticide/Nematicide SC/L (a liquid concentrate formulation containing 3.77 lb oxamyl active ingredient per U.S. gallon) were made to cotton at 1.0 lb ai/A/application, with a retreatment interval (RTI) of 5-7 days, resulting in a total application rate of 3 lb ai/A which is equal to the maximum label rate. All applications were made in spray volumes of 20 to 30 gal/A. The third and final application was made 14 days before harvest of seed cotton (14 day PHI) which is shortest PHI allowed.

Duplicate treated seed cotton samples were collected from three sites using picker harvesting equipment and treated seed cotton samples were harvested from three sites using stripper harvesting equipment. Untreated and treated samples were sent to Crop Guard Research, Inc. for processing into cotton gin by-products. Then the cotton gin by-product samples were sent to Morse Laboratories, Inc., where samples were subjected to further grinding and analyzed for moisture content. The maximum storage interval from sampling to extraction was 352 days (11.4 months).

Cotton gin by-product samples harvested from the field were stored frozen for up to 352 days (11.4 months) between harvest and extraction; all samples were analyzed within 6 days of extraction. A storage stability study was conducted concurrently with this study to determine the stability of oxamyl in cotton gin by-products stored frozen at -20°C ± 5°C. The storage stability study demonstrates that residues of oxamyl are stable in cotton gin by-products stored at -20°C ± 5°C for up to 14 months. No storage stability data on oxime residues were submitted in conjunction with this submission. However, available storage stability data for residues of oxamyl and its oxime metabolite in/on root crop vegetables (onions and potatoes), leafy vegetables (celery and mint), fruits and fruiting vegetables (apples, cucumbers, oranges, pineapple, and tomatoes), and oilseeds and nuts (cottonseed, peanuts, and soybeans) indicate that residues of oxamyl and its oxime metabolite are stable for at least 24 months of frozen storage in/on these commodities (Revised Residue Chemistry Chapter for the Oxamyl RED; DP# 267628, 7/25/00, J. Punzi). No additional storage stability data are required.

Cotton gin by-product samples were analyzed for residues of oxamyl and oxamyl oxime by LC/MS/MS method DuPont 11377 "Analytical Enforcement Method for the Determination of Oxamyl in Cotton Gin Trash Using LC/MS/MS." The method was validated prior to analysis of field trial samples. The limit of quantitation (LOQ) was 0.050 ppm for both oxamyl and oxamyl oxime in cotton gin by-products. The corresponding limit of detection (LOD) for both oxamyl and oxamyl oxime was defined as one-third the LOQ, or 0.02 ppm. Oxamyl oxime residues were converted to oxamyl equivalents, and added to residues of oxamyl found in each sample to give a total oxamyl equivalent value. The LC/MS/MS method was adequate for data collection based on concurrent method recoveries.

Briefly, oxamyl and its oxime metabolite were extracted from samples of cotton gin by-products with ethyl acetate. An aliquot was removed, passed through a pre-conditioned EnviCarb SPE cartridge and the eluate concentrated, diluted with acetone/cyclohexane and the solution passed through a pre-conditioned silica SPE cartridge. The silica cartridge was washed to remove impurities as oxamyl and oxamyl oxime were eluted. After concentration, residual organic solvent was removed, methanol was added, and samples were diluted with 10 mM acetic acid in preparation for LC/MS/MS analysis. The method separately determines residues of oxamyl and oxamyl oxime; residues of the oxime metabolite may be converted to oxamyl equivalents using a molecular weight conversion factor (1.35). The method is to be sensitive to oxamyl and its oxime metabolite at a limit of quantitation (LOQ) of 0.05 ppm and a limit of detection (LOD) was estimated at 0.02 ppm in cotton gin by-products. The method was adequately validated using samples of cotton gin by-products fortified at 0.05 through 40.0 ppm. Recoveries of oxamyl ranged from 80.8 to 120% (average 101 ± 12.2% standard deviation) and recoveries of oxamyl oxime ranged from 70.0 to 95.6% (82.7 ± 7.84%). The LC/MS/MS method uses a single ion transition to quantitate residues of oxamyl and oxamyl oxime in/on cotton gin by-product

matrices. For confirmation, the LC/MS/MS method may be used to monitor two parent-daughter ion transitions for each analyte: 237→72 and 237→90 for oxamyl, and 163→72 and 163→90 for the oxime.

Combined residues of oxamyl and oxime (as oxamyl equivalent) ranged from 6.2 to 40.7 ppm in cotton gin by-products following application at 3.0 lb ai/acre/season on seed cotton and collection at a PHI of 14 days; Table 1 contains the summary of field trial data.

TABLE 2. Residue Data from Crop Field Trials with Oxamyl

Trial ID (City, State; Year)	Crop; Variety	Commodity or Matrix	Total Rate lb ai/A (kg ai/ha)	PHI (days)	Residues (ppm)[1]		
					Oxamyl	Oxime (as Oxamyl Equiv.)	Total Oxamyl Equivalent[2]
Picker Cotton							
Elko, SC; 2001 (Site 1)	Cotton; D.P. 451	Cotton gin by-products	3.0 (3.36)	14	21.4, 23.0	4.2, 4.6	25.6, 27.6
Tillar, AR; 2001 (Site 2)	Cotton; Upland Cotton 451 BR	Cotton gin by-products	3.0 (3.36)	14	12.4[3], 10.6[3]	4.2[2], 3.4[2]	16.5, 14.0
Madera, CA; 2001 (Site 4)	Cotton; Riatta RR, Acala Cotton	Cotton gin by-products	3.0 (3.36)	14	35.4, 34.3	5.3, 5.5	40.7, 39.8
Stripper							
Eakly, OK; 2001 (Site 5)	Cotton; PM 2280 BG/RR	Cotton gin by-products	3.0 (3.36)	13	5.0, 10.1	1.2, 5.9	6.2, 16.0
Levelland, TX; 2001 (Site 6)	Cotton; Paymaster (PM 2326 B6/RR)	Cotton gin by-products	3.0 (3.36)	14	27.6, 26.7	2.8, 3.0	30.4, 29.7
Claude, TX; 2001 (Site 8)	Cotton; Paymaster (PM 2326 RR)	Cotton gin by-products	3.0 (3.36)	14	36.6, 38.8	1.0, 1.1	37.6, 39.9

[1] The LOQ for oxamyl and oxamyl oxime was 0.05 ppm.
[2] Total Oxamyl Equivalents Found (ppm) = Oxamyl Amount Found (ppm) + Oxime Amount Found, Expressed as Oxamyl Equivalents (ppm).
[3] Values represent average of the initial analysis and re-analysis of the sample.

TABLE 2. Summary of Residue Data from Crop Field Trials with Oxamyl on Stripper Cotton.

Commodity	Total Applic. Rate lb ai/A (kg ai/ha)	PHI (days)	Analyte	Residue Levels (ppm)						
				N	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Cotton Gin By-Products	3.0 (3.36)	13-14	Oxamyl	6	5.0	38.8	37.7	27.2	24.1	13.8
			Oxime	6	1.0	5.9	3.6	24.1	2.5	1.9
			Total	12	6.2	39.9	38.8	30.1	26.6	13

Results and Discussion:

Based on the maximum combined residues of oxamyl and oxime in stripper cotton (6 residue data from 3 field trials, see attachment 1), a tolerance at 120 ppm in/on cotton gin-byproducts, calculated by NAFTA MRL calculator, is now required.

There were two issues of concern identified with this submission, one with respect to the impact of residues in/on cotton gin byproduct on livestock tissues and the other with data-collection method. These concerns are discussed below.

Impact on Livestock Tissues: As cotton gin-byproduct is only fed to beef cattle (at maximum of 10% of their diet as roughage), a potential effect on livestock tolerance requirement was considered. HED had concluded previously that there was no reasonable expectation of finite oxamyl residues of concern in animal commodities [40 CFR, §180.6(a)(3)]. The previously conservatively-calculated dietary burden for beef cattle (L.Cheng, D209731, 6/25/1996) was 1.21 ppm based on 50% peanut hay and 15% soybean meal. Adding 13.3 ppm contribution from cotton gin by-product in beef cattle diet (120 ppm X 10% / 90% DM = 13.3 ppm) to the previously calculated dietary burden brings the total to only 14.51 ppm. This conservative maximum dietary burden is approximately half of the feeding level in goat metabolism study (31 ppm) in which no detectable residues of oxamyl and its oxime were found in any tissue. Therefore, HED maintains that there is no reasonable expectation of finite oxamyl residues of concern in animal commodities [40 CFR, §180.6(a)(3)].

Concern With Data-Collection Method - Comparison of the GLC enforcement method (MRM cited in PAM II) to the LC/MS/MS method DuPont 11377 used for analyzing cotton gin byproduct samples which does not involve any alkaline hydrolysis step, originally raised a concern as to whether the DuPont 11377 method is able to release any conjugated oxamyl or oxime identified in the plant metabolism study (see Registration Standard, 1/30/1987).

Briefly, the enforcement method for plant commodities is a GLC method with flame photometric detection (sulfur mode) listed in the Pesticide Analytical Manual (PAM) Vol.II, Method I. This method involves initial ethyl acetate extraction, followed by water extraction and alkaline hydrolysis to convert oxamyl to the oxime metabolite, therefore, the method determines combined residues of oxamyl and its oxime metabolite. By contrast, the LC/MS/MS method DuPont 11377 used for analyzing cotton gin byproduct samples which does not involve any alkaline hydrolysis step.

It was found that in the plant metabolism studies the oxime glucose (also called oximino dimethyl glucose) conjugates are only released from post-extraction solids (PES) fraction after enzymatic or acid hydrolyses and are not soluble in ethyl acetate. Therefore, it is believed that no significant amount, if any of the bound oxime conjugates is released by the GLC enforcement method. It should be also noted that the 2000 MARC memorandum (D260911, 1/5/2000) indicates that the oxime metabolite is not likely to be a potent acetyl cholinesterase inhibitor and keeping the metabolie in the tolerance expression is only because the enforcement method converts oxamyl to oxime residues. It also adds that the concentrations of oxamyl reported by these methods will include an unknown amount of oxime; consequently, both oxamyl and oxime metabolite will be included in the tolerance expression.

Based on the above findings, this reviewer concludes that the LC/MS/MS method DuPont 11377 used for analyzing cotton gin byproduct samples is acceptable as data-collection method for cotton gin byproducts since the underestimation of the residues, if any, would be very minor. In addition, use of LC/MS/MS method DuPont 11377 for cotton gin byproduct is not going to impact HED previous conclusion of no reasonable expectation of finite oxamyl residues of concern in animal commodities [40 CFR, §180.6(a)(3)]; back calculation shows that the level of total oxime residues must >270 ppm in/on cotton gin byproduct before secondary residues on livestock tissues are expected. However, since the extraction solvent used in DuPont method 11377 is quite different than that used in tolerance enforcement method and plant metabolism study and also does not involve a hydrolysis step, should the registrant wish to use this method as data-collection for other commodities in future, an acceptable radiovalidation of this method or a side-by-side comparison of this method with GLC enforcement method should be conducted; it is recommended that the registrant conduct such analyses on one of the matrices used in the plant metabolism study and has shown to be the most challenging for analysis.

Attachment 1: Residue Data and MRL Calculator Results.

Attachment 1: Residue Data and MRL Calculator Results.

Regulator:	EPA
Chemical:	Oxamyl
Crop:	Cotton Gin Byproduct
PHI:	14 day
App. Rate:	3.0 lb ai/ A
Submitter:	DuPont

Residues (stripper cotton gin byproduct)
6.2000
16.0000
30.4000
29.7000
37.6000
39.9000

	Regulator:	EPA	
	Chemical:	Oxamyl	
	Crop:	Cotton Gin Byproduct	
	PHI:	14 day	
	App. Rate:	3.0 lb ai/ A	
	Submitter:	DuPont	
	n:	6	
	min:	6.20	
	max:	39.90	
	median:	30.05	
	average:	26.63	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I	50	60	70
Normal	(75)	(95)	(--)
95/99 Rule	75	**120**	210
	(320)	(840)	(--)
EU Method II		80	
Distribution-Free			
Mean+3SD		**70**	
UCLMedian95th		**240**	
Approximate		0.8126	
Shapiro-Francia	p-value > 0.05 : Do not reject lognormality assumption		
Normality Test			

Oxamyl/DPX-D1410/PC Code 103801/E. I. du Pont de Nemours and Company
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3
Crop Field Trial – Cotton Gin By-Products

Primary Evaluator — Date: 29-JUL-2010

Mohsen Sahafeyan, Chemist
Risk Assessment Branch 1 (RAB1)
Health Effects Division (HED; 7509P)

Approved by — Date: 29-JUL-2010

Felecia Fort, Chief
RAB1/HED (7509P)

Note: This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 06/11/10). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

45803801. Nathan, Edward C. III (2002) Magnitude of Residues of Oxamyl in Cotton Gin By-Products Following Application of Vydate® C-LV Insecticide/Nematicide at Maximum Label Rates. DuPont Study No. DuPont-6624. Unpublished study prepared by E. I. du Pont de Nemours and Company. 129 pages.

EXECUTIVE SUMMARY:

E. I. du Pont de Nemours and Company has submitted field trial data for oxamyl in cotton gin by-products. A total of six field trials were conducted in the United States during the 2001 growing season. The trials took place in Region 2 (1 trial in SC), Region 4 (1 trial in AR), Region 6 (1 trial in OK), Region 8 (2 trials in TX), and Region 10 (1 trial in CA). Two additional trial sites were established in Region 8 as backup sites, however, samples from these sites were not analyzed. One treated plot and one untreated control plot were established at each trial site. At each trial, three broadcast applications of Vydate® C-LV Insecticide/Nematicide SC/L (a liquid concentrate formulation containing 3.77 lb oxamyl active ingredient per U.S. gallon) were made to cotton at 1.0 lb ai/A/application, with a retreatment interval (RTI) of 5-7 days, resulting in a total application rate of 3 lb ai/A. All applications were made in spray volumes of 20 to 30 gal/A. The third and final application was made 14 days before harvest of seed cotton (14 day PHI).

Duplicate treated seed cotton samples were collected from three sites using picker harvesting equipment and treated seed cotton samples were harvested from three sites using stripper harvesting equipment. Two of the fields were designated as backup sites; samples from these trials were not needed. Untreated and treated samples were sent to Crop Guard Research, Inc. for processing into cotton gin by-products. Then the cotton gin by-product samples were sent to Morse Laboratories, Inc., where samples were subjected to further grinding and analyzed for moisture content.

Cotton gin by-product samples were analyzed for residues of oxamyl and oxamyl oxime by LC/MS/MS method DuPont 11377 "Analytical Enforcement Method for the Determination of Oxamyl in Cotton Gin Trash Using LC/MS/MS." The method was validated prior to analysis of field trial samples. The limit of quantitation (LOQ) was 0.050 ppm for both oxamyl and oxamyl oxime in cotton gin by-products. The corresponding limit of detection (LOD) for both oxamyl and oxamyl oxime was defined as one-third the LOQ, or 0.02 ppm. Oxamyl oxime residues were converted to oxamyl equivalents, and added to residues of oxamyl found in each sample to give a total oxamyl equivalent value. The LC/MS/MS method was adequate for data collection based on concurrent method recoveries.

Cotton gin by-product samples harvested from the field were stored frozen for up to 352 days (11.4 months) between harvest and extraction; all samples were analyzed within 6 days of extraction. A storage stability study was conducted concurrently with this study to determine the stability of oxamyl in cotton gin by-products stored frozen at -20°C ± 5°C (46091101.der). The storage stability study demonstrates that residues of oxamyl are stable in cotton gin by-products stored at -20°C ± 5°C for up to 14 months. Available storage stability data on other crops support the storage duration and condition for oxamyl and oxime residues under frozen condition for up to 24 months.

Combined residues of oxamyl and oxime (as oxamyl equivalent) ranged from 6.2 to 40.7 ppm in cotton gin by-products following application at 3.0 lb ai/acre/season on seed cotton and collection at a PHI of 14 days.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP # 372355.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The study described was conducted to meet the requirements of EPA Good Laboratory Practice Standards (40 CFR Part 160) with the following exceptions:

1. Weather data were not collected under GLP standards.
2. Pesticide and fertilizer history for the test sites were provided by the growers; applications were not necessarily made under GLP standards.
3. Soil characterization was not conducted under GLP standards.
4. Tank mixtures were not analyzed for uniformity.
5. Only one empty test substance container was retained. All other empty containers were destroyed.
6. Characterization of the test substance for identity, strength, purity, and composition was performed before the start of the study. Stability was performed concurrently with the study.

None of these reported deviations from regulatory requirements had an impact on the validity of the study.

A. BACKGROUND INFORMATION

Oxamyl, also known as DPX-D1410, is an insecticide/nematicide used for control of insects and nematodes in cotton production. Oxamyl is registered for use on apples, bananas, carrots, celery, citrus, cotton, cucumbers, eggplants, garlic, ginger, muskmelon (including cantaloupe and honeydew melon), onion (dry bulb), peanuts, pears, peppers, peppermint, pineapples, plantains, potatoes, pumpkins, soybeans, spearmint, squash, sweet potatoes, tobacco, tomatoes, watermelons, yams, and non-bearing apple, cherry, citrus, peach, and pear to control insects, mites, and/or nematodes.

The chemical structure and nomenclature of oxamyl and its oxime metabolite are summarized in Table A.1, and the physicochemical properties of oxamyl are summarized in Table A.2.

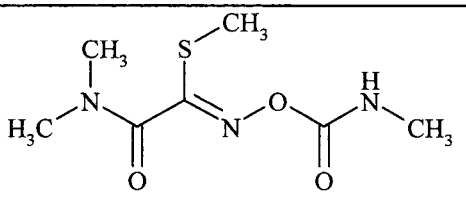
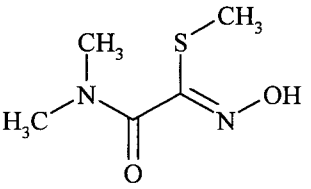
Table A.1. Oxamyl and Its Oxime Metabolite Nomenclature.	
Chemical structure	
Common name	Oxamyl
Company experimental name	DPX-D1410
IUPAC name	*N, N*-dimethyl-2-methylcarbamoyloxyimino-2-(methylthio)acetamide
CAS name	Methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate
CAS #	23135-22-0
End-use product/EP	3.77 lb/gal SC/L formulation (Vydate® C-LV Insecticide/Nematicide)
Chemical structure	
Common Name	Oxime
Company experimental name	DPX-A2213
CAS name	Methyl 2-(dimethylamino)-*N*-hydroxy-2-oxoethanimidothioate
CAS #	66344-33-0

Table A.2. Physicochemical Properties of Technical Grade Oxamyl.		
Parameter	Value	Reference
Melting range	97-100 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
pH	3.4	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Density	bulk: 0.34 g/mL absolute: 0.97 g/mL	
Water solubility	28 g/100 g at 25 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
Solvent solubility	at 25 °C Methanol 130 g/100 g Acetone 67 g/100 g Ethanol 33 g/100 g Toluene 1 g/100 g	
Vapor pressure	2.3×10^{-4} mm Hg @ 25 °C	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Dissociation constant, pK_a	non-ionic; no acidic or basic properties	
Octanol/water partition coefficient, $Log(K_{OW})$	K_{ow} = 0.36 at 25 °C	
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Refer to Table B.1.1 for trial site conditions and Table B.1.2 for study use patterns, and Table B.1.3 for trial numbers and geographical locations.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: City, State, Country; Year (Trial No.)	Soil characteristics			
	Type	% OM[1]	pH	CEC[2] (meq/g)
Elko, SC, USA; 2001 (1)	Loamy Sand	0.8	6	Not provided
Tillar, AR, USA; 2001 (2)	Silt Loam	1.7	6.9	Not provided
Madera, CA, USA; 2001 (4)	Loam	1.9	7.1	Not provided
Eakly, OK, USA; 2001 (5)	Sandy Loam	0.6	5.4	Not provided
Levelland, TX, USA; 2001 (6)	Sandy Loam	0.8	8.2	Not provided
Claude, TX, USA; 2001 (8)	Silty Loam	1.5	7.0	Not provided

[1] OM = Organic Matter
[2] CEC = Cation Exchange Capacity

Climate, soil type, and other conditions were typical of areas where oxamyl insecticide/nematicide may be used to control insects in cotton production. All test sites were large enough to allow normal, commercial ground application and nonsystematic collection of samples. Maintenance chemicals used at each trial site during the study were reported. Except for minor differences noted in the appendix of the study report, temperatures and rainfall were within normal historical limits. Rainfall was supplemented with irrigation as needed.

TABLE B.1.2. Study Use Pattern.

Location City, State; Yr (Trial No.)	EP[1]	Application						Tank Mix/ Adjuvant	Harvest Procedures
		Method	Timing	Volume[2] GPA	Rate lb a.i./A (kg ai/ha)	RTI[3] (days)	Total Rate lb a.i./A (kg ai/ha)		
Elko, SC; 2001 (1)	Vydate® C-LV	Foliar broadcast spray	maturing cotton (35-60% open bolls)	20.2	1.0 (1.12)	NA	3.0 (3.36)	None	Mechanical picker
				20.6	1.0 (1.12)	6			
				20.4	1.0 (1.12)	6			
Tillar, AR; 2001 (2)	Vydate® C-LV	Foliar broadcast spray	maturing cotton (10-60% open bolls)	21.1	1.0 (1.12)	NA	3.0 (3.36)	None	Mechanical picker
				21.1	1.0 (1.12)	6			
				19.5	1.0 (1.12)	7			
Madera, CA; 2001 (4)	Vydate® C-LV	Foliar broadcast spray	maturing cotton (boll opening)	30.0	1.0 (1.12)	NA	3.0 (3.36)	None	Mechanical picker
				30.0	1.0 (1.12)	5			
				30.0	1.0 (1.12)	6			
Eakly, OK; 2001 (5)	Vydate® C-LV	Foliar broadcast spray	maturing cotton (30-60% open bolls)	24.3	1.0 (1.12)	NA	3.0 (3.36)	None	Stripper
				23.5	1.0	6			

TABLE B.1.2. Study Use Pattern.

Location City, State; Yr (Trial No.)	EP [1]	Application						Tank Mix/ Adjuvant	Harvest Procedures
		Method	Timing	Volume[2] GPA	Rate lb a.i./A (kg ai/ha)	RTI[3] (days)	Total Rate lb a.i./A (kg ai/ha)		
					(1.12)				
				23.5	1.0 (1.12)	6			
Levelland, TX; 2001 (6)	Vydate® C-LV	Foliar broadcast spray	maturing cotton (60-80% open bolls)	20.0	1.0 (1.12)	NA	3.0 (3.36)	None	Stripper
				20.0	1.0 (1.12)	6			
				20.3	1.0 (1.12)	6			
Claude, TX; 2001 (8)	Vydate® C-LV	Foliar broadcast spray	maturing cotton (BBCH 87/89/90)	20.8	1.0 (1.12)	NA	3.0 (3.36)	None	Stripper
				21.2	1.0 (1.12)	7			
				21.1	1.0 (1.12)	6			

[1]EP = End-use Product; Vydate® C-LV SC/L formulation [3.77 lb oxamyl/U.S. gallon water-soluble liquid concentrate]
[2] GPA = Gallons per acre
[3] Retreatment Interval.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Cotton Gin By-Products		
	Submitted	Requested	
		Canada	U.S.
1			
1A			
2	1		1
3			
4	1		1
5			
5A			
5B			
6	1[1]		1
7			
7A			
8	2[2]		2
9			
10	1		1
11			
12			
13			
14			
15			
16			
17			
18			

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Cotton Gin By-Products		
	Submitted	Requested	
		Canada	U.S.
19			
20			
21			
Total	6[1]		6

[1] The study report lists one location (Eakly, OK) as being in Region 6, but according to the region descriptions in the OPPTS 860.1500 guidelines, the trial location is actually in Region 8, approximately 13 miles from Region 6. Due to the close proximity to Region 6, the trial location is still represented as Region 6 in this DER.
[2]Two additional field sites were established in Region 8 as back-up sites. Samples collected from these sites were not analyzed.

B.2. Sample Handling and Preparation

One sample of seed cotton was collected from the control plot, and two replicate samples of seed cotton were collected from the treated plot at each test site. The samples were collected 13-14 days following the final application of the test substance. Each seed cotton sample generated using mechanical picker equipment (test sites 1,2,4) consisted of a minimum weight of 130 lb. Each seed cotton sample where cotton was harvested with stripper equipment (test sites 5,6,8) was approximately 75 lb. All samples were collected nonsystematically, starting with the control plot and ending with the treated plot. The samples were labeled with study, test, and treatment numbers, sample date, PHI, and unique identification number.

Seed cotton samples were bagged, identified, and shipped directly from the field to Crop Guard Research, Inc., for ginning. Samples for this study consisted of picked or stripped seed cotton from which cotton gin by-product samples were generated by a specific cleaning and processing procedure, with ginning at one facility (Crop Guard Research, Inc., Colony, OK) and further grinding/homogenization at another facility (Morse Laboratories, Inc., Sacramento, CA). Seed ginning procedures followed commercial procedures described in the Crop Guard Research Standard Operating Procedure "Sample Cotton Gin and Gin Trash (Bur) Extractor Operation." Any deviations from processing protocols were minor and had no impact on the study. Consistent with normal commercial practice, all samples were shipped to the processing facility at ambient temperature and stored at ambient temperature prior to ginning. All seed cotton samples were ginned within 1 day of receipt. Crop Guard Research, Inc. ginned one control and two treated seed cotton samples from field test sites 1, 2, 4, 5, 6, and 8 to generate cotton gin by-product samples for analysis.

All cotton gin by-product samples were frozen within 2 hours at -10°C or colder and retained frozen until shipped to Morse Laboratories, Sacramento, CA via A.C.D.S. freezer trucks for further processing. At Morse Laboratories, Inc., cotton gin by-product samples were removed from frozen storage and ground/homogenized in preparation for sample analysis and determination of moisture content of selected samples. To expedite sample analysis, all ground cotton gin by-product samples were then shipped frozen by Federal Express to the DuPont Stine-Haskell Research Center. All samples arrived in acceptable frozen condition, and were stored frozen at -20°C ± 5°C prior to extraction and analysis.

B.3. Analytical Methodology

Cotton gin trash samples were analyzed for oxamyl and oxamyl oxime following the draft method DuPont -11377 "Analytical Enforcement Method for the Determination of Oxamyl in Cotton Gin Trash Using LC/MS/MS".

Oxamyl and its oxime were extracted from samples of cotton gin by-products with ethyl acetate. An aliquot was removed, passed through a pre-conditioned ENVI-Carb SPE cartridge, and the eluate concentrated, diluted with acetone/cyclohexane and the solution passed through a pre-conditioned silica SPE cartridge. The silica cartridge was washed to remove impurities, and oxamyl and oxamyl oxime were eluted. After concentration, residual organic solvent was removed, methanol was added, and samples were diluted with water in preparation for LC/MS/MS analysis. Oxamyl and its oxime were separated from co-extractants with reversed-phase liquid chromatography, using an Agilent Hypersil ODS HPLC column. Analysis was performed using a Micromass Quattro II triple quadrapole LC/MS/MS instrument with an electrospray ionization (ESI) source operated in MS/MS-(MRM) positive ion mode. Oxamyl oxime residues were converted to oxamyl equivalents and added to oxamyl residues to provide total oxamyl equivalent values.

The analytical method was validated prior to analysis of field-treated samples. The validation samples were fortified with oxamyl and oxamyl oxime, extracted, processed, and analyzed for oxamyl and oxamyl oxime using the same methods as for the field-treated test samples. Control cotton gin by-product samples collected from Test Site 5 were used for method validation. One analytical set, consisting of one unfortified control sample, two control samples fortified at the anticipated Limit of Quantitation (LOQ) (0.050 ppm), and two control samples fortified at 10 times that level (0.5 ppm), was used for method validation.

The Limit of Quantitation (LOQ) for oxamyl and oxamyl oxime in cotton gin by-products was determined to be 0.05 ppm. The LOD for oxamyl was 0.02 ppm. The signal-to-noise response for oxamyl oxime was generally equal to or higher than for oxamyl, so for analysis of oxamyl oxime in cotton gin by-products, the LOQ for oxamyl oxime was defined as the lowest fortification level analyzed where recoveries routinely fell in the range of 70 to 120% with an RSD less than 20%, or 0.050 ppm. The LOD for oxamyl oxime was at least 0.02 ppm or lower (defined as one-third the LOQ).

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage interval from sampling to extraction was 352 days (11.4 months). All sample extracts were analyzed within 6 days of extraction. A storage stability study was conducted concurrently with this study to determine the stability of oxamyl in cotton gin by-products stored frozen at -20°C ± 5°C. A storage stability study was conducted concurrently with this study to determine the stability of oxamyl in cotton gin by-products stored frozen at -20°C ± 5°C. The storage stability study demonstrates that residues of oxamyl are stable in cotton gin by-products stored at -20°C ± 5°C for up to 14 months. Available storage stability data on other crops indicate the stability of oxamyl and its oxime residue under frozen condition for up to 24 months.

Concurrent method recovery data are shown in Table C.1. The LC/MS/MS method was adequate for data collection based on concurrent method recoveries. Control samples were fortified with oxamyl and oxamyl oxime at 0.05, 20 ppm, and 40 pm and analyzed concurrently with unfortified controls and treated samples to verify method performance. The fortification levels tested bracketed the range of residue values detected. All concurrent method recoveries were between the acceptable range of 70-120%. One unfortified control sample showed interference; this value was not included in the average of the 0.050 ppm fortification samples. Data from the analysis of unfortified and fortified control samples validated method performance.

Residue data from the field trials are reported in Table C.3. A summary of the residue data is presented in Table C.4. Combined residues of oxamyl and oxime (as oxamyl equivalent) range from 6.2 to 40.7 ppm in cotton gin by-products following application at 3.0 lb ai/A (PHI 14 days).

TABLE C.1. Summary of Concurrent Recoveries of Oxamyl and its Oxime.

Matrix	Analyte	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev[2] (%)
Cotton Gin By-Products	Oxamyl	0.05	2	148[1], 108, 104	106
		20.0	3	104, 117, 120	114±8.6
		40.0	2	106, 110	108
	Oxime	0.05	2	83[1], 86, 70	78
		20.0	3	85, 76, 81	81±4.7
		40.0	2	74, 77	76

[1] This fortification recovery value was not included in average due to contamination in the control sample.
[2] Standard deviation was calculated for sample size greater than n=2.

TABLE C.2. Summary of Storage Conditions.

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Interval[1]	Interval of Demonstrated Storage Stability[2]
Cotton Gin By-Products	Oxamyl	≤-20±5	323-352 days (10.4-11.4 months)	14 months
	Oxamyl Oxime			Data not available

[1] Actual storage duration from harvest to sample extraction. All samples were analyzed within 6 days of extraction.
[2] Refer to storage stability DER for MRID 46091101.

TABLE C.3. Residue Data from Crop Field Trials with Oxamyl

Trial ID (City, State; Year)	Crop; Variety	Commodity or Matrix	Total Rate lb ai/A (kg ai/ha)	PHI (days)	Residues (ppm)[1]		
					Oxamyl	Oxime (as Oxamyl Equiv.)	Total Oxamyl Equivalent[2]
Elko, SC; 2001 (Site 1)	Cotton; D.P. 451	Cotton gin by-products	3.0 (3.36)	14	21.4, 23.0	4.2, 4.6	25.6, 27.6
Tillar, AR; 2001 (Site 2)	Cotton; Upland Cotton 451 BR	Cotton gin by-products	3.0 (3.36)	14	12.4[3], 10.6[3]	4.2[2], 3.4[2]	16.5, 14.0
Madera, CA; 2001 (Site 4)	Cotton; Riatta RR, Acala Cotton	Cotton gin by-products	3.0 (3.36)	14	35.4, 34.3	5.3, 5.5	40.7, 39.8
Eakly, OK; 2001 (Site 5)	Cotton; PM 2280 BG/RR	Cotton gin by-products	3.0 (3.36)	13	5.0, 10.1	1.2, 5.9	6.2, 16.0
Levelland, TX; 2001 (Site 6)	Cotton; Paymaster (PM 2326 B6/RR)	Cotton gin by-products	3.0 (3.36)	14	27.6, 26.7	2.8, 3.0	30.4, 29.7
Claude, TX; 2001 (Site 8)	Cotton; Paymaster (PM 2326 RR)	Cotton gin by-products	3.0 (3.36)	14	36.6, 38.8	1.0, 1.1	37.6, 39.9

[1] The LOQ for oxamyl and oxamyl oxime was 0.05 ppm.
[2] Total Oxamyl Equivalents Found (ppm) = Oxamyl Amount Found (ppm) + Oxime Amount Found, Expressed as Oxamyl Equivalents (ppm).

[3] Values represent average of the initial analysis and re-analysis of the sample.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Oxamyl.

Commodity	Total Applic. Rate lb ai/A (kg ai/ha)	PHI (days)	Analyte	Residue Levels (ppm)						
				N	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Cotton Gin By-Products	3.0 (3.36)	13-14	Oxamyl	12	5.0	38.8	37.7	22.2	21.8	11.6
			Oxime	12	1.0	5.9	5.4	3.7	3.6	1.6
			Total [2]	12	6.2	40.7	40.3	26.6	25.3	11.5

[1] HAFT = Highest Average Field Trial
[2]Total combined oxamyl and oxamyl oxime residues in parent equivalents.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of Vydate® C-LV Insecticide/Nematicide on seed cotton, which was harvested at normal maturity and ginned to produce cotton gin by-products. A maximum seasonal application rate of 3 lb ai/A of oxamyl was used, from three 1 lb ai/A applications, with an application interval of 6 days between applications, and harvest of seed cotton 14 days following the final, third application. Samples of the cotton gin by-products were analyzed, and residues of oxamyl and oxamyl oxime were determined. Total oxamyl equivalent residues in/on cotton gin by-products ranged from 6.2 to 40.7 ppm.

Based on concurrent recoveries, an acceptable method was used for the quantitation of oxamyl in cotton gin by-products, and acceptable data were generated. Adequate storage stability is available for oxamyl to support the storage durations and conditions of samples from the submitted crop field trial study. Although, no storage stability data were submitted for residues of oxime in cotton gin by-products in conjunction with this study, available storage stability data on other crops indicate that oxamyl and oxime residues are stable under frozen condition for up to 24 months.

There were no unusual weather conditions reported that may have adversely impacted the results of the study. Additionally, it does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#: 157409
Subject: Oxamyl Product Chemistry Standard Update. CBRS # 7201
From: E. Zager
To: L. Rossi and R. Engler
Dated: 6/18/91
MRID(s): 40499701, 40499702, 40499704, 40790001, and 41118201

DP#: 263858
Subject: Oxamyl. List A Reregistration Case 0253. PC Code 103901. REVISED Product Chemistry Chapter for the Reregistration Eligibility Decision (RED) Document – Comments on du Pont's "Gross" Errors-only 2/18/00 Response.
From: K. Dockter
To: C. Jarvis
Dated: 3/15/00
MRID(s): 450453-00 to -05

F. DOCUMENT TRACKING

RDI: RAB6 Chemists
Petition Number(s): None
DP Barcode(s): 372355
PC Code: 103801

Template Version June 200

Oxamyl/DPX-D1410/PC Code 103801/E. I. du Pont de Nemours and Company
DACO 7.3/OPPTS 860.1380/OECD IIA 6.1.1 and IIIA 8.1.1
Storage Stability – Cotton Gin By-Products

Primary Evaluator — Date: 29-JUL-2010

Mohsen Sahafeyan, Chemist
Risk Assessment Branch 1 (RAB1)
Health Effects Division (HED; 7509P)

Approved by — Date: 29-JUL-2010

Felecia Fort, Chief
RAB1/HED (7509P)

Note: This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 06/11/10). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46091101. McClory, J. and R. Henze, (2003). Magnitude of Residues of Oxamyl in Cotton Gin By-Products Following Application of Vydate® C-LV Insecticide/Nematicide at Maximum Label Rates. Project Identification No.: DuPont-6624, Supplement No. 1. Unpublished study prepared by E.I. DuPont de Nemours and Company. 41 pages.

45803801. Nathan, Edward C. III (2002) Magnitude of Residues of Oxamyl in Cotton Gin By-Products Following Application of Vydate® C-LV Insecticide/Nematicide at Maximum Label Rates. DuPont Study No. DuPont-6624. Unpublished study prepared by E. I. du Pont de Nemours and Company. 129 pages.

EXECUTIVE SUMMARY:

E.I. DuPont de Nemours and Company has submitted the results of a storage stability study with oxamyl in cotton gin by-products (trash). The study was started concurrently with the crop field trial on cotton gin by-products (MRID 45803801) and was completed in the supplemental study MRID 46091101. Untreated samples of cotton gin by-products were fortified with oxamyl at a nominal fortification level of 0.50 ppm. Samples were placed in frozen storage at -20±5°C and analyzed at nominal storage intervals of 0, 1, 4, 9, or 14 months.

Cotton gin by-product samples were analyzed for oxamyl using the draft method of DuPont-11377, "Analytical Enforcement Method for the Determination of Oxamyl in Cotton Gin Trash Using LC/MS/MS." The limit of quantitation (LOQ) for oxamyl was experimentally determined to be 0.050 ppm. The limit of detection (LOD) for oxamyl was 0.02 ppm. The analytical method was found to be adequate based on method validation and concurrent recoveries.

The storage stability data are adequate and reflect that frozen storage stability has been demonstrated for residues of oxamyl in/on cotton gin by-products for up to 418 days (14 months) of freezer storage at -20±5°C.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP # 372355.

COMPLIANCE:

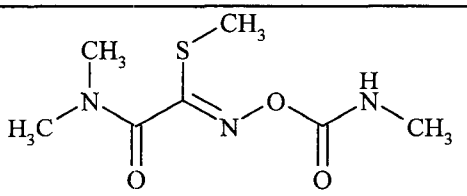
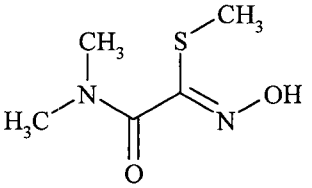
Signed and dated Good Laboratory Practice (GLP), Quality Assurance and No Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Oxamyl, also known as DPX-D1410, is an insecticide/nematicide used for control of insects and nematodes in cotton production. Oxamyl is registered for use on apples, bananas, carrots, celery, citrus, cotton, cucumbers, eggplants, garlic, ginger, muskmelon (including cantaloupe and honeydew melon), onion (dry bulb), peanuts, pears, peppers, peppermint, pineapples, plantains, potatoes, pumpkins, soybeans, spearmint, squash, sweet potatoes, tobacco, tomatoes, watermelons, yams, and non-bearing apple, cherry, citrus, peach, and pear to control insects, mites, and/or nematodes.

The chemical structure and nomenclature of oxamyl and its oxime metabolite are summarized in Table A.1, and the physicochemical properties of oxamyl are summarized in Table A.2.

Table A.1. Oxamyl and Its Oxime Metabolite Nomenclature.

Chemical structure	
Common name	Oxamyl
Company experimental name	DPX-D1410
IUPAC name	*N, N*-dimethyl-2-methylcarbamoyloxyimino-2-(methylthio)acetamide
CAS name	Methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate
CAS #	23135-22-0
End-use product/EP	3.77 lb/gal SC/L formulation (Vydate® C-LV Insecticide/Nematicide)
Chemical structure	
Common Name	Oxime
Company experimental name	DPX-A2213
CAS name	Methyl 2-(dimethylamino)-*N*-hydroxy-2-oxoethanimidothioate

CAS #	66344-33-0

Table A.2. Physicochemical Properties of Technical Grade Oxamyl.

Parameter	Value	Reference
Melting range	97-100 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
pH	3.4	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Density	bulk: 0.34 g/mL absolute: 0.97 g/mL	
Water solubility	28 g/100 g at 25 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
Solvent solubility	at 25 °C Methanol 130 g/100 g Acetone 67 g/100 g Ethanol 33 g/100 g Toluene 1 g/100 g	
Vapor pressure	2.3×10^{-4} mm Hg @ 25 °C	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Dissociation constant, pK_a	non-ionic; no acidic or basic properties	
Octanol/water partition coefficient, $Log(K_{OW})$	K_{ow} = 0.36 at 25 °C	
UV/visible absorption spectrum	Not available	

Source: DP#337527, William D. Wassell

B. EXPERIMENTAL DESIGN

B.1. Sample Handling and Preparation

Control samples of cotton gin by-product were acquired from the magnitude of residue trials conducted in South Carolina (Site 1) and Texas (Site 6), as described in MRID 45803801. With the exception of the samples used to determine the one-month storage interval, the samples were prepared for frozen storage stability testing at Morse Laboratories, Inc. Cotton gin by-product samples were received by Morse Laboratories in good frozen condition and were stored frozen at -20±5°C. Samples were prepared by grinding with dry ice using a Reitz Disintegrator. Each sample was mixed extensively to ensure homogeneity. Samples were spiked with oxamyl at a nominal fortification level of 0.50 ppm. The stock solutions were prepared using methanol as the solvent. No information was provided on the stability of the solution. Samples were shipped frozen (on dry ice) by Federal Express from Morse Laboratories to the DuPont Stine-Haskell Research Center for analysis. Upon arrival, samples were stored at -20±5°C prior to extraction and analysis. Samples used for the one-month storage interval were prepared and analyzed at the DuPont Stine-Haskell facility.

Samples analyzed during method validation at the Stine-Haskell Research Center were used as the 0-day storage stability samples. The analytical set consisted of two samples fortified at 0.50 ppm, two samples fortified at 0.05 ppm (LOQ), and one unfortified control. For the other storage analysis intervals (1, 4, 9, and 14 months), two storage samples fortified with 0.50 ppm

20

oxamyl (aged samples), two samples freshly fortified at 0.50 ppm oxamyl (method verification samples) and one unfortified control sample were analyzed. It should be noted that Table 1 on Page 23 of MRID 46091101 indicates that one of the two fresh fortified samples were spiked with oxamyl oxime and analyzed for oxamyl. This is assumed to be an error and that the sample was spiked with oxamyl, as indicated in the text on page 18 of MRID 46091101.

B.2. Analytical Methodology

Cotton gin by-product samples were analyzed for oxamyl following the draft method DuPont - 11377 "Analytical Enforcement Method for the Determination of Oxamyl in Cotton Gin Trash Using LC/MS/MS" (46091102.der).

Oxamyl was extracted from samples of cotton gin by-products with ethyl acetate. An aliquot was removed, passed through a pre-conditioned ENVI-Carb SPE cartridge, and the eluate concentrated, diluted with acetone/cyclohexane and the solution passed through a pre-conditioned silica SPE cartridge. The silica cartridge was washed to remove impurities, and oxamyl and oxamyl oxime were eluted. After concentration, residual organic solvent was removed, methanol was added, and samples were diluted with water in preparation for LC/MS/MS analysis.

The analytical method was validated prior to analysis of field-treated samples at 0.05 ppm and 0.50 ppm using control samples from Test Site 5. These samples were also used for the Day 0 storage stability samples. The LOQ of the analytical method for the determination of oxamyl was experimentally determined to be 0.050 ppm. The LOD for oxamyl was 0.02 ppm, one-third the LOQ.

C. RESULTS AND DISCUSSION

Concurrent method recovery data and the results of the storage stability data are presented in Table C.1. Average concurrent recoveries from the samples analyzed with the 1, 4, 9, and 14 months storage stability samples ranged from 86% to 103%. The concurrent recovery data indicate that the method is adequate for the determination of oxamyl in cotton gin by-products. Apparent residues in control samples were <LOQ and adequate example chromatograms were provided.

The results of the storage stability study are presented in Table C.2. In cotton gin by-products stored frozen at approximately -20±5°C, average corrected recoveries of oxamyl were 87.4% on Day 0, 109% on Day 136, 98% on Day 262, and 103% on Day 418.

Based on the reported data, residues of oxamyl are stable in/on cotton gin by-products for up to 418 days (14 months) when stored in freezer at -20±5°C.

A graph of the storage stability of residues of oxamyl is presented in Figure C.1.

TABLE C.1. Summary of Concurrent Recoveries of Oxamyl from Cotton Gin By-Product.

Matrix	Spike level (ppm)	Storage Interval[1] (months)	Sample size (n)	Recoveries (%)	Mean ± std dev[2] (%)
Oxamyl					
Cotton Gin By-Product	0.50	1 (31 days)	2	103, 102	103
	0.50	4 (136 days)	2	116, 76.2	96.2
	0.50	9 (262 days)	2	101, 102	101
	0.50	14 (418 days)	2	84.2, 87.5	85.8

[1] Samples analyzed during method validation were used as the 0-day storage stability samples. The analytical set consisted of two samples fortified at 0.50 ppm, two samples fortified at 0.05 ppm (LOQ), and one unfortified control. The results from the samples fortified at 0.50 ppm are shown in Table C.2.
[2] It should be noted that Table 1 on Page 23 of MRID 46091101 indicates that the first of the two fresh fortified samples were spiked with oxamyl oxime and analyzed for oxamyl. This is assumed to be an error and that the sample was actually spiked with oxamyl, as indicated in the text on page 18 of MRID 46091101.
[2]Standard deviations for mean values were not calculated because the number of individual values used to calculate the mean was less than three.

TABLE C.2. Stability of Oxamyl Residues in Cotton Gin By-Product Following Storage at -20±5°C.

Commodity	Spike level (ppm)	Storage interval[1,2] (months)	Recovered residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[3]
Oxamyl						
Cotton Gin By-Product	0.50	0	0.404, 0.471	0.437	87.4	NA
	0.50	1 (31 days)	0.479, 0.477	0.478	95.7	93.0
	0.50	4 (136 days)	0.488, 0.557	0.522	104	109
	0.50	9 (262 days)	0.513, 0.478	0.496	99.1	98.0
	0.50	14 (418 days)	0.430, 0.453	0.441	88.3	103

[1] Samples analyzed during method validation were used as the 0-day storage stability samples. The analytical set consisted of two samples fortified at 0.50 ppm, two samples fortified at 0.05 ppm (LOQ), and one unfortified control. The results from the samples fortified at 0.50 ppm are shown in this table.
[2] The number of days is calculated from date of sample preparation through extraction. Samples were analyzed 0 to 2 days after extraction.
[3] Corrected for mean concurrent recovery (see TABLE C.1.).

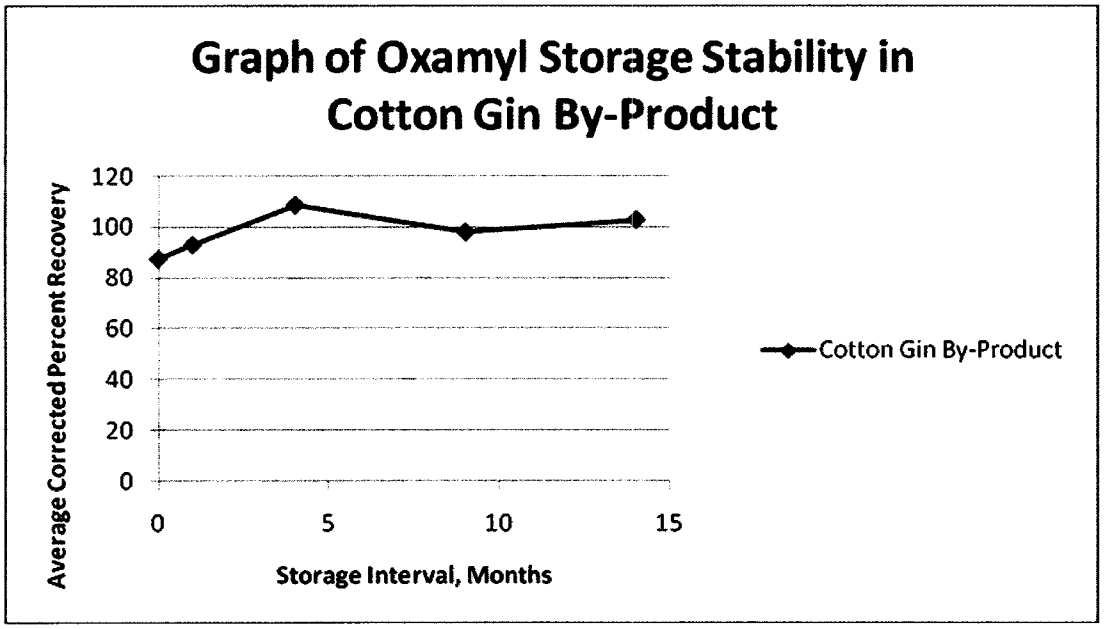


Figure C.1. Graph of Oxamyl Storage Stability in Cotton Gin By-Product

D. CONCLUSION

The submitted storage stability results adequately demonstrate the stability of residues of oxamyl stored frozen for up to 14 months. An acceptable method was used for the quantitation of residues in the tested commodity.

E. REFERENCES

DP#s: 337527
Subject: "Magnitude and Decline of Oxamyl Residues in Sugarbeet Roots and Tops Following Applications of Dupont™ Vydate® C-LV Insecticide/Nematicide - U.S. 2005"
From: William D. Wassell
To: George F. Kramer
Dated: 9/11/07
MRIDs: 46980506

Revised Residue Chemistry Chapter for the Oxamyl Reregistration Eligibility Decision (RED) Document, J. Punzi, 7/25/00, DP#: 267628.

F. DOCUMENT TRACKING

RDI: RAB6 Chemists
Petition Number(s): None
DP Barcode(s): 372355
PC Code: 103801

Oxamyl/DPX-D1410/PC Code 103801/ E. I. du Pont de Nemours and Company
DACO 7.2.1, 7.2.2, and 7.2.3/OPPTS 860.1340/OECD IIA 4.2.5, 4.2.6 and 4.3
Residue Analytical Method – Cotton Gin By-Products

Primary Evaluator — Date: 29-JUL-2010

Mohsen Sahafeyan, Chemist
Risk Assessment Branch 1 (RAB1)
Health Effects Division (HED; 7509P)

Approved by — Date: 29-JUL-2010

Felecia Fort, Chief
RAB1/HED (7509P)

Note: This Data Evaluation Record (DER) was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 6/11/10). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46091102. McClory J.P., R.M. Henze, (2003) Analytical Enforcement Method for the Determination of Oxamyl and its Oxime Metabolite in Cotton Gin By-products Using LC/MS/MS. DuPont Study Number: 11377. Unpublished study prepared by E. I. du Pont de Nemours and Company. 51 p.

EXECUTIVE SUMMARY:

E. I. du Pont de Nemours and Company (DuPont) has submitted a liquid chromatograph with tandem mass spectrometers (LC/MS/MS) method (DuPont-11377 Revision No. 1), for the determination of residues of oxamyl and its metabolite oxime in/on cotton gin by-products. This method was used for data collection in samples from cotton gin by-products submitted in conjunction with DP# 372355.

Briefly, parent oxamyl and its oxime metabolite were extracted from samples of cotton gin by-products with ethyl acetate. An aliquot was removed, passed through a pre-conditioned EnviCarb SPE cartridge and the eluate concentrated, diluted with acetone/cyclohexane and the solution passed through a pre-conditioned silica SPE cartridge. The silica cartridge was washed to remove impurities as oxamyl and oxamyl oxime were eluted. After concentration, residual organic solvent was removed, methanol was added, and samples were diluted with 10 mM acetic acid in preparation for LC/MS/MS analysis.

The method is to be sensitive to oxamyl and its oxime metabolite at a limit of quantitation (LOQ) of 0.05 ppm and a limit of detection (LOD) was estimated at 0.02 ppm in cotton gin by-products. The method was adequately validated using samples of cotton gin by-products fortified at 0.05 through 40.0 ppm. Recoveries of oxamyl ranged 80.8 to 120% (average 101 ± 12.2% standard deviation) and recoveries of oxamyl oxime ranged 70.0 to 95.6% (82.7 ± 7.84%).

The LC/MS/MS method uses a single ion transition to quantitate residues of oxamyl and oxamyl oxime in/on cotton gin by-product matrices. For confirmation, the LC/MS/MS method may be used to monitor two parent-daughter ion transitions for each analyte: 237→72 and 237→90 for oxamyl, and 163→72 and 163→90 for the oxime.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical methods data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 372355.

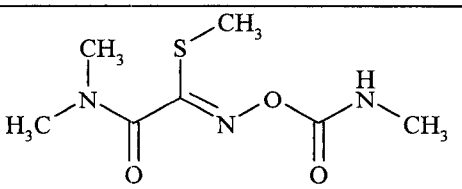
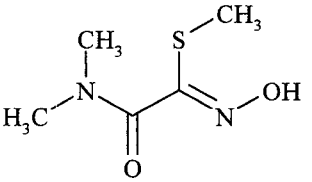
COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Oxamyl is a carbamate insecticide, acaricide, and nematocide; a revised residue chemistry chapter for the Oxamyl RED was issued 7/25/2000. Oxamyl is registered for use on apples, bananas, carrots, celery, citrus, cotton, cucumbers, eggplants, garlic, ginger, muskmelon (including cantaloupe and honeydew melon), onion (dry bulb), peanuts, pears, peppers, peppermint, pineapples, plantains, potatoes, pumpkins, soybeans, spearmint, squash, sweet potatoes, tobacco, tomatoes, watermelons, yams, and non-bearing apple, cherry, citrus, peach, and pear to control insects, mites, and/or nematodes.

The chemical structure and nomenclature of oxamyl and its oxime metabolite are presented in Table A.1, and the physicochemical properties of the technical grade of oxamyl are presented in Table A.2.

Table A.1. Oxamyl and Its Oxime Metabolite Nomenclature.	
Chemical structure	
Common name	Oxamyl
Company experimental name	DPX-D1410
IUPAC name	*N, N*-dimethyl-2-methylcarbamoyloxyimino-2-(methylthio)acetamide
CAS name	Methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate
CAS #	23135-22-0
End-use product/EP	3.77 lb/gal SC/L formulation (DuPont™ Vydate® C-LV Insecticide/Nematicide; EPA Reg. No. 352-532)
Chemical structure	
Common Name	Oxime
Company experimental name	DPX-A2213

CAS name	Methyl 2-(dimethylamino)-*N*-hydroxy-2-oxoethanimidothioate
CAS #	66344-33-0

Table A.2. Physicochemical Properties of Technical Grade Oxamyl.

Parameter	Value	Reference
Melting range	97-100 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
pH	3.4	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Density	bulk: 0.34 g/mL absolute: 0.97 g/mL	
Water solubility	28 g/100 g at 25 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
Solvent solubility	at 25 °C Methanol 130 g/100 g Acetone 67 g/100 g Ethanol 33 g/100 g Toluene 1 g/100 g	
Vapor pressure	2.3×10^{-4} mm Hg @ 25 °C	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Dissociation constant, pK_a	non-ionic; no acidic or basic properties	
Octanol/water partition coefficient, $Log(K_{OW})$	K_{ow} = 0.36 at 25 °C	
UV/visible absorption spectrum	Not available	

Source: DP#337527, William D. Wassell

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Cotton gin by-product samples from field trial studies associated with DP # 372355 were analyzed for residues of oxamyl and its metabolite oxamyl oxime using LC/MS/MS Method DuPont-11377 entitled "Analytical Enforcement Method for the Determination of Oxamyl and its Oxime Metabolite in Cotton Gin By-products Using LC/MS/MS."

The method submitted in this report is a slight modification to the original DuPont-11377 Method entitled "Analytical Enforcement Method for the Determination of Oxamyl in Cotton Gin Trash Using LC/MS/MS." The modification was made to improve the stability of oxamyl standard solutions by making them up in 10 mM acetic acid and recommending that a refrigerated auto-sampler be used for analysis.

B.1.1. Principle of Method DuPont-11377, Revision No. 1:

Parent oxamyl and its oxime metabolite were extracted from samples of cotton gin by-products with ethyl acetate. An aliquot was removed, passed through a pre-conditioned EnviCarb SPE cartridge and the eluate concentrated, diluted with acetone/cyclohexane and the solution passed through a pre-conditioned silica SPE cartridge. The silica cartridge was washed to remove impurities as oxamyl and oxamyl oxime were eluted. After concentration, residual organic

solvent was removed, methanol was added, and samples were diluted with 10 mM acetic acid in preparation for LC/MS/MS analysis.

The method separately determines residues of oxamyl and oxamyl oxime; residues of the oxime metabolite may be converted to oxamyl equivalents using a molecular weight conversion factor (1.35). The parameters of the method are described in Table B.1.1.

TABLE B.1.1. Summary Parameters for the Analytical Method Used for the Quantitation of Oxamyl and its Metabolite Oxime Residues in Cotton Gin By-Products.

Method ID	Dupont-11377
Analyte(s)	Oxamyl (DPX-D1410) Oxime (DPX-A2213)
Extraction solvent/technique	A 15 gram (g) sample is homogenized and then extracted with ethyl acetate. Tissuemize for 5 minutes and centrifuge for 10 minutes at 3000 rpm, decant, and repeat two more times.
Cleanup strategies	The extracts were passed through a pre-conditioned EnviCarb SPE column cartridge and the eluate was concentrated, diluted with 10/90 acetone/cyclohexane and the solution was passed through a pre-conditioned silica SPE cartridge. The eluate was concentrated, the residual organic solvent was removed, methanol was added, and the samples were diluted with 10 mM acetic acid in preparation for LC/MS/MS analysis.
Instrument/Detector	**HPLC** Hewlett-Packard HP1100 HPLC Chromatography Conditions Solvents: A: 1 mM Ammonium formate in 99:1 water:methanol B: 99:1 Methanol:water HPLC Column: Agilent Hypersil ODS, 2.1 mm i.d. x 10 cm, 3 µm diameter packing Injection Volume: 20 µL Gradient Program: Time (min) / %A / %B / Flow rate (mL/min) 0 / 100 / 0 / 0.30 13.0 / 74 / 26 / 0.30 13.1 / 10 / 90 / 0.30 17.0 / 10 / 90 / 0.30 17.1 / 100 / 0 / 0.30 25.0 / 100 / 0 / 0.30 **MS** Micromass Quattro II Triple Quadrapole Chromatography Conditions & GC/MS Run Parameters Scanning Mode: Multiple Reaction Monitoring (MRM), positive ion mode Electrospray Voltage: 4.58 kV Detector Voltage: 750 V Source Temperature: 150 °C Collision Gas Pressure: 2.2×10^{-3} mBar Nebulizing Gas Flow: 15 L/h Drying Gas Flow: 300 L/h
Standardization method	External standardization using standards of oxamyl and oxamyl oxime. The response factor is calculated as the ratio of the analyte concentration to the peak area.
Stability of std solutions	Standards should be freshly prepared monthly and stored at approximately 4°C immediately after each use. Standard solutions are stable for approximately 6 months when stored at 4°C immediately after use.
Retention times	Oxamyl Oxime: Approximately 8.0 min Oxamyl: Approximately 11.5 min

B.2. Enforcement Method

The enforcement method for plant commodities is a GLC method with flame photometric detection (sulfur mode) listed in the Pesticide Analytical Manual (PAM) Vol.II, Method I. This method involves initial ethyl acetate extraction, followed by water extraction and alkaline hydrolysis to convert oxamyl to the oxime metabolite, therefore, the method determines combined residues of oxamyl and its oxime metabolite.

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

The method validation recoveries of oxamyl and oxamyl oxime from fortified samples of cotton gin by-products were adequate. The method validation data are presented in Table C.1.1. The method characteristics for DuPont Method 11377 are presented in Table C.1.2. For confirmation, the LC/MS/MS method may be used to monitor two parent-daughter ion transitions for each analyte: 237→72 and 237→90 for oxamyl, and 163→72 and 163→90 for the oxime metabolite. For both oxamyl and oxime, the ion ratios of the fortified samples were within range of the standards and thereby provided confirmation.

TABLE C.1.1. Recovery Results from Method Validation of Cotton Gin By-Products using the Data-Gathering Analytical Method (LC/MS/MS Method DuPont-11377).[1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev.[2] (%)
Oxamyl			
Cotton Gin By-Products	0.05	86, 87.2, 109, 104	96.5 ± 11.6
	0.50	80.8, 94.2, 100, 101	94.2 ± 9.43
	20.0	104, 117, 120	114 ± 8.55
	40.0	110	110
Oxamyl Oxime			
Cotton Gin By-Products	0.05	80.2, 81.4, 86.0, 70.0	79.4 ± 6.75
	0.50	75.2, 87.8, 95.6, 95.6	88.6 ± 9.63
	20.0	85.5, 76.1, 81.4	81.0 ± 4.71
	40.0	77.4	77.4

[1] Fortification standards were prepared in a 5% methanol:95% 10 mM acetic acid solution.
[2] Standard deviation not applicable for sample sizes of less than 3 samples.

TABLE C.1.2. Characteristics for the Data-Gathering Analytical Method Used for the Quantitation of Oxamyl and its Metabolite Oxime Residues in Cotton Gin By-Products.

Analyte(s)	Oxamyl (DPX-D1410) Oxime (DPX-A2213)
Equipment ID	The method recommends the use of the following equipment: Hewlett-Packard HP1100 HPLC Micromass Quattro II Triple Quadrapole
LOQ	0.05 ppm
LOD	0.02 ppm
Accuracy/Precision	For the LC-MS/MS detector response to be considered accurate, the measured value at the LOQ or above should be within ± 20% of the nominal solution concentration.

Reliability of the Method/ [ILV]	Results from an ILV study are not provided in this study.
Linearity	Over the range of 0.5 ng/mL to 20.0 ng/mL, the method detector response is considered linear when the r^2=0.99 for the calibration curve and the relative standard deviation of the response factors consistently being less than 15%. A calibration curve was provided in this study.
Specificity	Chromatograms were provided for review in this study.

C.2. Enforcement Method

The enforcement method for plant commodities is a GLC method with flame photometric detection (sulfur mode) listed in the Pesticide Analytical Manual (PAM) Vol.II, Method I. This method involves initial ethyl acetate extraction, followed by water extraction and alkaline hydrolysis to convert oxamyl to the oxime metabolite, therefore, the method determines combined residues of oxamyl and its oxime metabolite..

C.3. ILV

An Independent Laboratory Validation study was performed using the original DuPont-11377 analytical method (refer to DER for MRID 46034901). A modification based on the results of the study was made to the original method in order to improve the stability of oxamyl standard solutions by making them up in 10 mM acetic acid and by recommending that a refrigerated auto-sampler be used for analysis.

D. CONCLUSION

The submitted LC/MS/MS method, DuPont Method 11377, is adequate for determining residues of oxamyl and oxamyl oxime in cotton gin by-products. Acceptable validation data have been submitted at fortification levels of 0.05 to 40.0 ppm for cotton gin by-products. An ILV study was submitted for cotton gin by-products (see DER for MRID 46034901) but was not reviewed for this DER. DuPont Method 11377 was revised slightly to address the recommendations from the ILV study. Because the method includes an alternate analysis with MS detection using a second daughter ion transition for each analyte, a separate confirmatory method or interference study is not required.

E. REFERENCES

DP#s: 337527
Subject: PP#6F7136. Oxamyl (Chemical No. 103801). Petition for the Establishment of Permanent Tolerances for Use on Sugar Beet. Summary of Analytical Chemistry and Residue Data.
From: W.D. Wassell
To: D. Rosenblatt and S. Brothers
Dated: 11-September, 2007
MRIDs: 46980502-04, 46980506, and 47008901

DP#s: None
Subject: Independent Laboratory Validation of Method Dupon-11377, "Analytical Enforcement Method for the Determination of Oxamyl and its Oxime Metabolite in Cotton Gin By-products Using LC/MS/MS DuPon-12688.
From: C.D. Chickering, ABC Laboratories, Inc.

Dated: July 2, 2003
MRID#: 46034901

F. DOCUMENT TRACKING

RDI: RAB6 Chemists
Petition Number(s): None
DP Barcode(s): 372355
PC Code: 103801

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Chemical Name: Oxamyl

PC Code: 103801
HED File Code: 11000 Chemistry Reviews
Memo Date: 7/29/2010
File ID: 00000000
Accession #: 000-00-0135

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